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Gestating at altitude: How do maternal physiology and evolutionary adaptation influence fetal growth?

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Gestating at altitude: How do maternal physiology and evolutionary adaptation influence fetal growth?

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Fetal growth is reduced for lowland mammals under hypoxia

- Lowland mammals experience increased risk for fetal growth restriction at high altitude, while altitude adapted animals mitigate altitude-induced reductions in fetal growth
- **Fetal growth is determined by maternal physiology and placental function**, but the underlying mechanisms for preservation of fetal growth under hypoxia are not yet understood

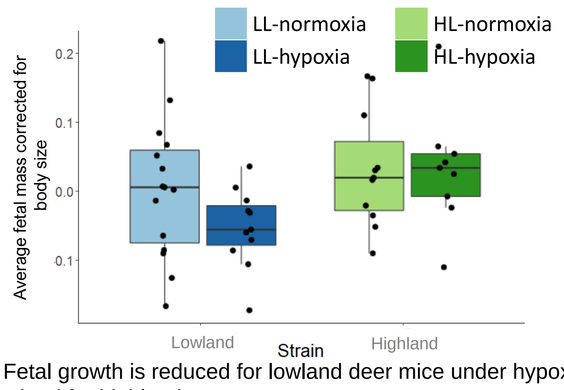
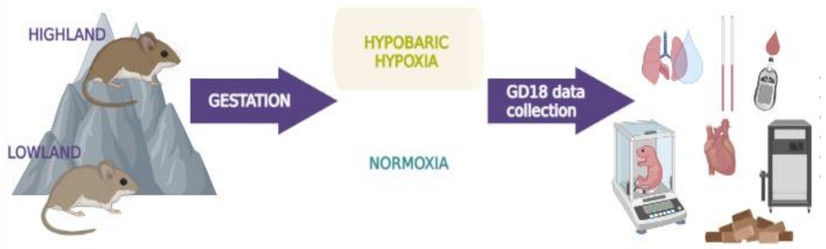


Figure 1 Fetal growth is reduced for lowland deer mice under hypoxia and maintained for highlanders

We hypothesized that altitude dependent changes in maternal physiology affect fetal growth phenotypes



- **Fetal masses**
- **Blood hematocrit, hemoglobin, & glucose**
- **Whole heart & right ventricle mass**
- **Wet & dry lung mass**
- **Body condition**
- **Food consumption**

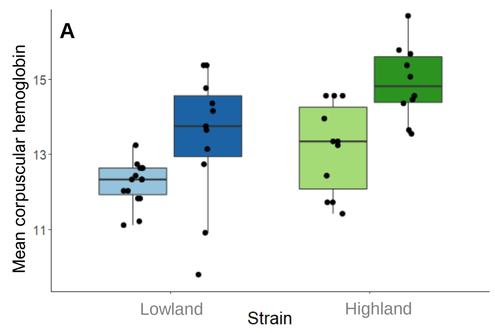
- Linear modeling and model comparison approaches were used to assess the relationships between maternal physiology and fetal growth
- To determine whether fetal growth is tied to a composite of changes in many aspects of maternal physiology, we used PCA to reduce dimensionality in a linear modeling framework

How is maternal physiology affected by altitude acclimation?

Cardiopulmonary physiology influences oxygen availability for fetal growth

Nonpregnant lowland deer mice display maladaptive cardiopulmonary responses under hypoxia
- increase Hct & Hb,
- exhibit lung edema & right ventricle hypertrophy

Nonpregnant highlanders suppress these cardiopulmonary responses



B

Outcome	Strain	Treatment	Strain*Treatment
Hematocrit			
Hemoglobin, g / dL			
Lung edema, g H_2O / g tissue			
Right ventricle hypertrophy, g RV / g whole heart			

Figure 2 A There is an effect of strain and an effect of hypoxia treatment on mean corpuscular hemoglobin, but no interaction of strain and treatment. **B** Output of multiple linear modeling; significance of predictors for each trait modeled reported. p < 0.05 in green, p > 0.05 in red

Cardiopulmonary responses to hypoxia are similar among highland and lowland deer mice during pregnancy

Energy use and allocation may limit fetal growth

Fetal growth deficiency may be related to insufficient energy allocation

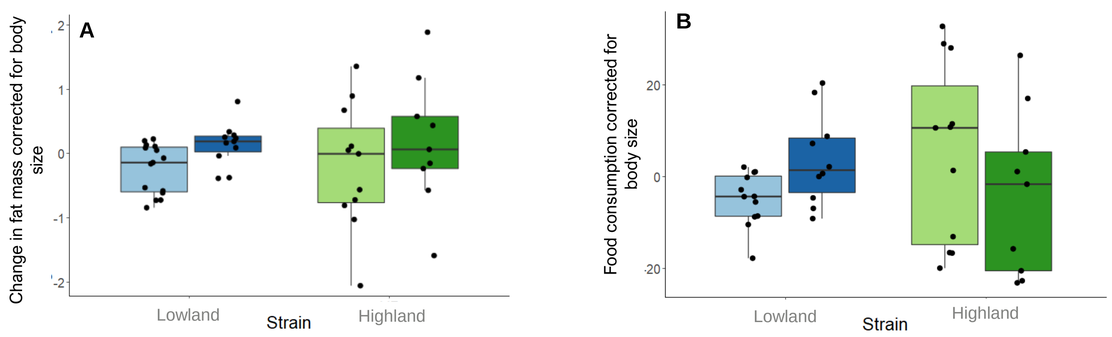


Figure 3 A There is a slight trend of increased change in fat mass for both strains under hypoxia (Treatment .05 < p < .1) **B** The effect of strain by treatment interaction for food consumption suggests that this differs for highland and lowland deer mice under hypoxia (Strain*treatment p = .055)

- Highlanders maintain fetal growth while reducing food intake without reducing fat mass

Highland deer mice under hypoxia may manage energy differently than lowlanders

Acknowledgements

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Do changes in maternal physiology contribute to fetal growth phenotype?

Maternal acclimation to hypoxia may explain fetal growth phenotypes

1. Individual maternal physiology traits may predict fetal growth outcomes

- Fetal growth was modeled as a function of maternal physiological variables and model fit was compared to a null model and a model including the experimental design using AICc

No maternal traits in isolation predict fetal growth

2. A composite of maternal physiology traits may predict fetal growth outcomes

- We reduced dimensionality using PCA (at right) which separates strains and treatments to some degree

Composite traits do not predict fetal growth

No predictors produced a model similar to or better than that provided by the **experimental design** when evaluated by model comparison

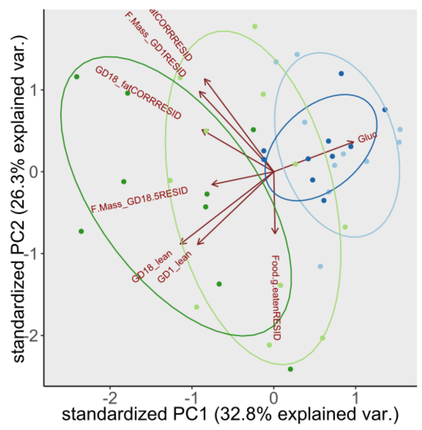

Figure 4 When plotted along PC1 and PC2, individuals in common groups vary together. These are primarily separated along variation in fat and lean mass, food consumption, and glucose. These composites do not predict fetal growth phenotype.

Maternal physiology does not predict fetal growth phenotype

Conclusions

Our results suggest that strain-specific changes in maternal physiology alone do not explain fetal growth under hypoxia

- **The use of data from a single gestational time point and imprecise measures (e.g., food consumption) may limit the strength of our results**
- **Maternal physiology may be tied to fetal growth phenotype, but the placenta is able to compensate**
- **Future work will examine the role of maternal physiology at an earlier developmental stage**
- **Data on energy use and allocation merits further attention through dedicated experiments**